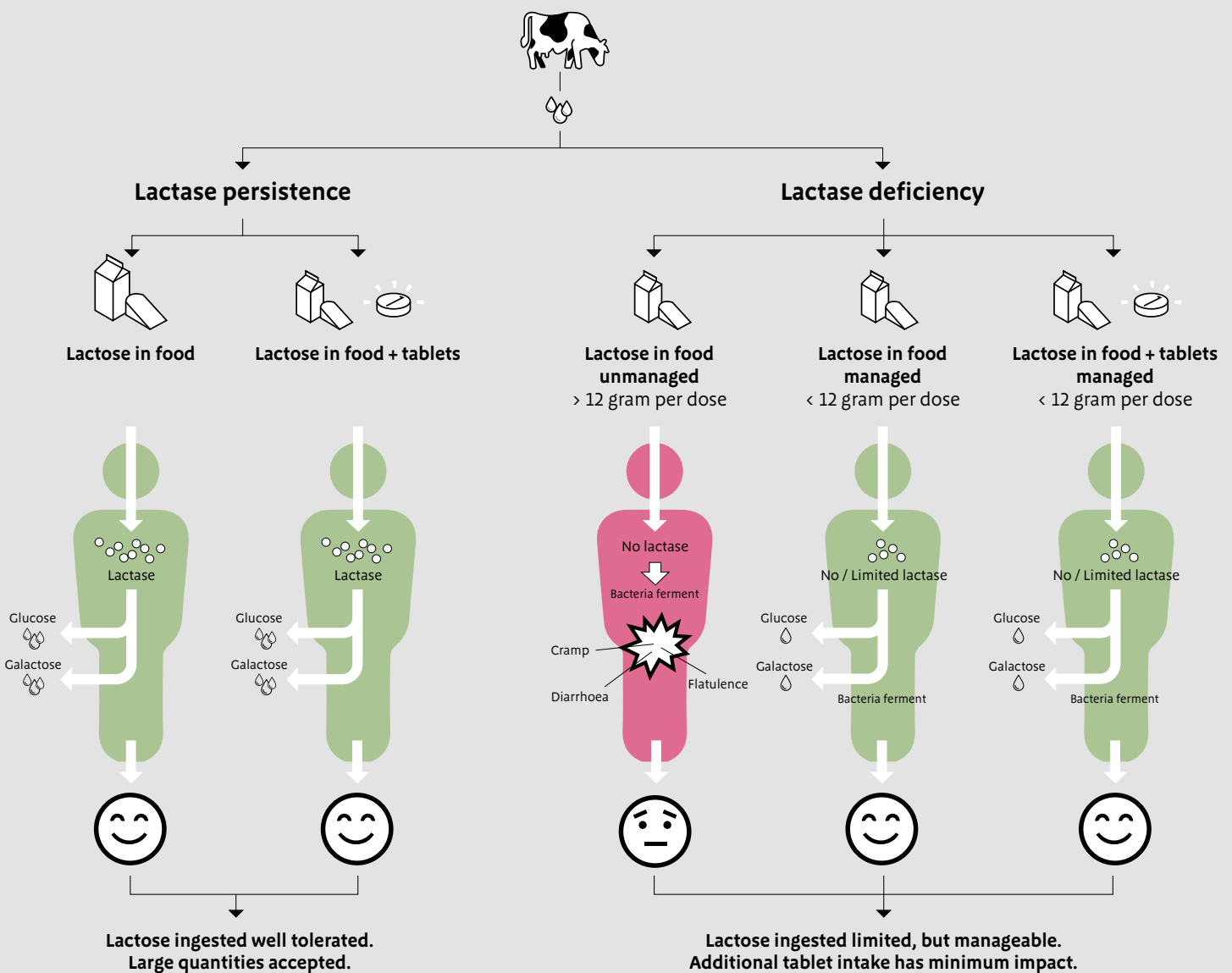


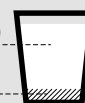


Lactose highly tolerated; based on ingested quantity



Glass of milk, 10,6 gram (88 %)

2 Tablets, 1,4 gram (12 %)



Identifying safe use of pharmaceutical lactose



This leaflet describes lactose intolerance being caused by lower than normal levels of the enzyme lactase in the gut, which makes it difficult for some patients to digest lactose, causing discomfort and other unpleasant symptoms. Medical researchers have studied how lactose intolerant patients respond to different levels of lactose, and published studies at last provide some real clarity about safe levels of exposure.

Pharmaceutical lactose is a very important (non-active) ingredient for use as an excipient in Oral Solid Dosage (OSD) medicines (Sommer D. et al., 2007) or as a carrier in dry powder inhalation, because it is stable, soluble and palatable. Yet most of the world's population has a form of lactose intolerance. The ability to digest lactose, the sugar found in the milk of all mammals, depends on the presence of lactase, which occurs naturally in babies and young children but tends to reduce with age. 70% of people across the world have reduced lactase in their gut by late childhood, and others develop lactase deficiency as they reach middle and late middle age (Hertzler S.R. et al., 1996; Heyman M.B. 2006). Lactose is broken down by lactase into its component monosaccharides: glucose and galactose, necessary to gain any nutritional benefit from lactose.

Yet low, or even no lactase production does not lead to complete intolerance of lactose. Lactose intolerance should also not be confused with milk allergy, which is a completely different condition caused by an adverse reaction to the proteins in cow's milk. This matters because patients today are becoming more active in researching their conditions and the medicines they are given, leading some lactose-intolerant individuals to assume, wrongly, that medicines containing lactose will cause unpleasant side-effects.

Safe usage: the scientific evidence

So what are the practical implications for pharmaceutical use of lactose, even for patients that have a very low level of lactase? Recent studies have investigated this question and there is now a strong consensus on the level of

lactose that it is safe for virtually all patients to consume, whether or not they are lactase deficient.

The scientific evidence suggests that between 6 and 12 grams of lactose can be taken by almost any patient with no ill effects. As the dosage increases, so an increasing number of lactase deficient patients may experience the classic symptoms that accompany fermentation of lactose in the large intestine: flatulence, stomach cramps and potential diarrhoea (Bril S. et al., 2011).

Reactions to lactose will vary, depending on whether food is eaten at the same time as medication is taken, as this normally reduces the likelihood of symptoms, and are also related to the frequency and number of tablets taken (Sommer D. et al., 2007; Montalto M. et al., 2008). To put this into perspective, if a glass of milk (250 ml) delivers the total acceptable dose of lactose (12 grams), two tablets that use lactose as an excipient deliver between 0.4 and 1.4 grams of lactose which is at most 12% of the acceptable limit and normally much less (Silanikove N. et al., 2015).

Recent literature shows evidence that 12 grams of pharmaceutical lactose in a single dosage, and 18 grams in a day, can be tolerated by virtually any human being, regardless of whether they have a lactase deficiency or not. (Corgneau M. et al., 2017 ; Smollich M., 2016). To go beyond this limit it would be necessary to take a very large number of tablets with a lactose excipient. This is rarely necessary and, in these unusual cases, clinicians will exercise caution in the formulation of the drugs they prescribe.

Lactose has been one of the most widely-used and successful excipients in pharmaceutical history. Recent research shows that even patients producing very low levels of lactase, or none at all, will experience no ill-effects from taking medicines that contain lactose as an excipient. The scientific evidence confirms safety and viability of lactose for the future.

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Prof. Dr Martin Smollich, 2016, Fortbildungskongress Schladming